

A Retrospective Mortality Study among Canadian Petroleum Marketing and Distribution Workers

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We conducted a retrospective mortality study among 6672 petroleum marketing and distribution workers from 226 locations throughout Canada. These employees worked for at least 1 year in the marketing distribution segment from 1964 through 1983 or were annuitants as of 1964. Industrial hygienists assigned hydrocarbon (HC) exposure frequency scores for several jobs, departments, and job functions. We computed standardized mortality ratios for the total cohort, HC exposure frequency groups, and tank truck drivers, and we also used Poisson regression techniques to model mortality for selected causes of death according to HC exposure frequency. Results indicate overall mortality below that of the general Canadian population for all marketing distribution workers [Standardized mortality ratio (SMR) = 0.88]. Mortality from aortic aneurysms was significantly elevated in all marketing/distribution workers (SMR = 1.79) but was due to raised mortality in nonexposed workers (SMR = 2.80). Tank truck drivers showed significantly elevated mortality due to leukemia (SMR = 3.35) based on five deaths. The leukemia findings were not evident in the larger group of marketing distribution workers classified as exposed to hydrocarbons (SMR = 1.01). No other cause of death was elevated in truck drivers. The leukemia findings are suggestive of a possible influence due to exposure to HCs in tank truck drivers, although other explanations cannot be ruled out. Other findings of elevated mortality in the marketing distribution group are generally not statistically significant. These included moderately increased mortality due to multiple myeloma, malignant melanoma, and kidney cancer. Small numbers of observed and expected deaths limit concise interpretations for these diseases.

Introduction

Little is known about the long-term health effects of petroleum products such as gasoline, diesel fuel, etc., in those who handle these substances, either occupationally or more generally. Most epidemiologic studies of oil industry employees have examined refinery workers (1). Refinery workers experience a wide range of hydrocarbon exposures from raw material in the form of crude oil to finished products such as gasoline and diesel fuel. Employees involved in the distribution of finished product are exposed to fewer potential hydrocarbon streams and offer an opportunity to study the health effects of substances to which more nonoccupational groups are exposed. There have been few of these studies in the literature.

Based on epidemiologic studies to date, two disease groups merit special attention in populations exposed to finished petroleum products: the lymphohematopoietic (LH) cancers and kidney cancer. A previous study was performed on the parent cohort of the population to be studied in this paper (2). This study found moderately raised mortality for multiple myeloma [observed deaths (O) = 7, standardized mortality ratio (SMR) = 1.81] for all male marketing/distribution workers and similar results (O = 5, SMR = 1.94) for males who were ever exposed to hydrocarbons. Neither SMR nor the aggregate mortality for males and females (O = 8, SMR = 1.89) was significant. More importantly, however, mortality excesses for multiple myeloma were higher for employees with long tenure and latencies as measured from date of first employment. Results from the same study for an aggregate category of LH cancers (non-Hodgkin's lymphoma, leukemia, multiple myeloma, and myelofibrosis) showed a slightly raised SMR of 1.24 based on 28 cases. Rushton and Alderson (3) found a similar result for this aggregate category (SMR = 1.15 based on 57 cases) including a slightly elevated multiple myeloma SMR of 1.17 (based on 11 deaths) in a study among U.K. distribution workers. However, these investigators do report that another lymphopoietic disorder, myelofibrosis, showed a significant

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SMR of 2.76, based on five cases, and cancer of other lymphoid tissue showed a moderately elevated SMR (1.65) based on six cases ($p = 0.16$).

Christie et al. (4) studied an Australian petroleum industry population that covers production, refining, and distribution of petroleum and its products. They reported a significant excess of myeloid leukemia (standardized incidence ratio [SIR] = 4.0) and nonsignificant elevations in multiple myeloma (SIR = 2.2) and non-Hodgkin's lymphoma (SIR = 1.7). Similar patterns were observed for mortality (5), except that myeloid leukemia mortality was not significant. Thus, there are inconsistent results for the LH cancers in distribution workers, though some significant excesses of different diseases have been reported.

Among refinery workers, who are exposed to a wider array of hydrocarbon streams besides fuels, a few epidemiologic studies have suggested that the mortality rate of LH cancers is above general population rates. One study reported a statistically significant excess for the category of all LH cancer (6). This study, along with another (7), also showed a statistically significant SMR for leukemia. Several studies have shown nonstatistically significant elevations for the category of "other LH cancer" (usually unspecified lymphomas, multiple myeloma, and polycythemia vera) (3,6-11).

Because high benzene exposures are known to cause acute myelogenous leukemia (AML) and because benzene is present in certain refinery streams, some studies have examined the risk of AML in refinery workers. Three studies found an SMR for AML below 1.0 (3,12,13), two found nonstatistically significant SMRs of 1.33 (6) and 1.07 (14), and one found a statistically significant SMR of 3.94 based on eight cases (7).

In addition, two nested case-control studies have examined a possible link between benzene and leukemia in refinery workers. One study (15) did not find any relationship to benzene. The other study (16) reported a positive relationship between the risk of leukemia and jobs involving "medium to high" benzene exposure. Thus, as with distribution workers, the literature suggests mixed results for the risk of leukemia and other LH cancers in refinery workers.

Kidney cancer is the other disease that may merit special attention in workers exposed to finished petroleum products. This finding primarily stems from bioassay results in the male rat. McFarland et al. (17) reported that male rats exposed to wholly vaporized unleaded gasoline experienced a dose-related increase in the incidence of renal carcinomas. Short et al. (18) pointed out many similarities between light hydrocarbon nephropathy in the male rat, which is due to a unique sex- and species-related protein ($\alpha_2\mu$ -globulin), and the renal tumors observed by McFarland (17). Loury et al. (19) and others have concluded that the tumorigenic effect in male rats occurs by mechanisms related to recurrent nephrotoxicity and cell turnover, which may not be relevant to humans.

Two epidemiologic studies in marketing/distribution workers suggest slightly raised mortality for kidney cancer, though neither risk is large nor statistically significant. For the parent population, the kidney cancer SMR

was 1.34 (2), and Rushton and Alderson (3) reported a similar result (SMR = 1.21) in U.K. distribution centers. Neither of these studies presented results by latency or duration, however. Thus, a higher risk in some worker subgroups cannot be ruled out.

Epidemiologic studies in refinery workers have generally shown little if any elevation in risk due to kidney cancer. These include several retrospective cohort mortality studies (6,8-12,20), as well as a multicompany case-control study that examined the risk of nonaromatic gasoline distillates among 102 renal cancer cases and 408 controls. Poole et al. (21) reported an odds ratio of 1.0 for exposure to these distillates. One exception to the lack of risk is a recent study (14) conducted on three U.S. refinery/chemical plant complexes. This study reported elevated mortality (SMR = 2.46) among blue collar workers at one refinery/chemical plant complex with a 95% confidence interval (CI) of 1.46-3.90. However, the two other complexes showed SMRs consistent with expectation.

The objective of this study was to describe mortality patterns in a group of Canadian marketing/distribution workers with potential exposure to finished petroleum products. Special attention was given to the LH cancers and kidney cancer.

Methods

Population Definition

The study population consists of all active employees and living retirees on 1 January 1964 and all new regular employees hired between 1 January 1964 and 31 December 1983 of a large Canadian petroleum company. One year of work in the marketing/distribution operating segment was necessary before an employee was included in this cohort. We excluded 1869 female employees who ever worked in distribution because very few of them ($n = 87$) were exposed to finished petroleum products, and only one exposed female died during the follow-up period. The definition of the study population was primarily driven by the availability of a computerized employee relations database, which is used for payroll and benefits purposes within the company.

The study population is a subset of a population (called the parent population in this paper) previously described (2). That study considered an employment criterion of 1 year at any location in the organization. These include locations in operating segments in addition to marketing/distribution, such as refining, upstream, and office. For our study, we restricted the population to males who worked at least 1 year in marketing/distribution ($n = 6672$) and the subset of these employees who were classified as ever exposed to hydrocarbons in the marketing/distribution segment ($n = 4889$). The previous report referred to this operating segment as marketing/transportation (2).

Several computerized and manual consistency checks were performed in constructing the total parent population. These included quality control checks on death coding, exposure coding consistency checks, and verification

of cohort eligibility. Two hundred random records were checked with hard-copy records. Date of birth and date of employment showed 100% and 99% agreement. Both date of employment disagreements were less than 1 year. A high degree of population completeness is necessary for payroll and benefits functions, although we did not formally test whether the population identified was complete.

The population includes employees from 226 marketing/distribution locations located throughout Canada. These locations represent nine provinces and the Northwest Territories. The distribution of the locations by province is shown in Table 1.

Work History Summarization

Work history records were also obtained from the computerized database. Work history fields included location, department, job title, and a code for job function, which was later used in assigning hydrocarbon exposure categories. The quality of work history information varied from location to location. The company began to implement the computerized database in 1960, and it covered all employees by 1964. However, each location varied as to the year they began entering complete work history information. Most locations began entering complete information sometime between 1960 and 1964, but we noted some incompleteness when examining manual records up until 1968 for the marketing/distribution segment. It is possible that the work history information is less reliable in this segment because it comprises numerous smaller locations.

For employees who quit before 1964 ($n = 2529$), only the last line of work history was captured and was assumed to be representative of their complete work history. The likely magnitude of this error is discussed later. For other employees whose date of first employment preceded their first work history entry ($n = 778$), we assumed that their first work history represented their work history from date of employment to the first entry. There were an average of 4.0 work history entries for each employee.

All changes in location, department, job title, and job function were included in the study data, along with the effective date of the change. All location/department combinations were reviewed by three industrial hygienists and assigned to an operating segment (e.g., refining, marketing/distribution, upstream, etc.). Assignment to the marketing/distribution segment was the basis for

selecting the population in this study. Generally, there was little movement between operating segments.

Hydrocarbon Exposure and Job Titles

Five company industrial hygienists were supplied with lists of unique work history entries and asked to assign each entry according to frequency of exposure to hydrocarbons (HCs) in the marketing/distribution segment. Two covered the eastern provinces and Quebec, one covered Ontario, and two covered the western provinces (British Columbia, Alberta, Saskatchewan, Manitoba, and the Northwest Territories). The industrial hygienists were asked to simply estimate if a given job title/function/department combination at a given location entailed exposure to hydrocarbons on a daily basis, on a less frequent (less than daily) basis, or not at all. Dermal and inhalation exposures to all forms of HCs, including combustion products, were considered. For marketing/distribution workers, HC is usually encountered through inhalation during product transfer operations. This estimate does not take into account intensity of exposure. The three groups are referred to as daily exposed, less than daily exposed, and nonexposed.

To assure consistency in the exposure rankings, entries with identical department/job function designations but different HC exposure scores were recycled to the industrial hygienists involved. This resulted in either a rationale for the disagreement (e.g., the same job function entailed different tasks at different locations) or reassignment of one of the HC exposure scores.

We did not systematically examine mortality by job titles. There are several hundred job titles represented in the database. Many of the job titles are unique, apparently defined and used by only one location. However, because tank truck drivers may have been exposed to HC levels above those of other workers in this cohort and were represented by relatively few job title entries, it was possible to define a list of these employees (called drivers). With the aid of company human resource specialists and industrial hygienists, we defined a group of 1453 employees who were ever drivers and examined the mortality experience of this group separately. The drivers in the company also frequently loaded fuel onto trucks, except at very large terminals, where the loading task was performed by loaders.

Vital Status Tracing

Records for all employees who were not active in 1983 nor receiving company benefits were sent to Statistics Canada (SC) for vital status tracing. Internal company databases as well as the U.S. National Death Index were also used to identify deaths, although 96% of the deaths (in the parent cohort) were identified through SC. Employee records that did not match SC's database were assumed to be alive until the end of the study. The effect of this important assumption was evaluated previously (22) by testing the method of death ascertainment with known deaths. An underascertainment of 2.4% was found for the

Table 1. Number of marketing/distribution locations by province.

Province	Number	Percent
Ontario	59	26
Quebec	51	23
British Columbia	30	13
Manitoba	23	10
Alberta	21	9
Nova Scotia	20	9
Saskatchewan	15	7
New Brunswick	3	1
Prince Edward Island	2	1
Northwest Territories	2	1
Total	226	100

Canadian deaths from the parent cohort, suggesting that the SMRs in this study are slight underestimates.

Death certificates were coded to the revision in effect of the International Classification of Diseases (ICD) coding scheme by SC. For the small percentage of deaths not identified by SC, a certified nosologist determined the underlying cause of death from the death certificate. There were seven deaths identified in this cohort (0.6% of total) with an unknown cause; these are counted in total mortality only.

Statistical Analyses

Each person contributed person-years from 1 January 1964 or the date in which 1 year of downstream employment was achieved, whichever was later. For two employees in which company records and SC records disagreed, we stopped person-years on the date of last employment and assigned vital status as unknown. We used the Monson program (23) to enumerate person-years to the earliest of date of death, the end of the follow-up period (31 December 1983), or the date of last employment for unknowns. Canada's Laboratory Center for Disease Control (LCDC) provided mortality rates and ICD/LCDC rate translation tables. Expected deaths were calculated by multiplying the Canadian national rates by the study person-year distributions by gender and by age and year quinquennia. Confidence intervals were calculated only if either the observed or expected number of deaths was at least 5.0, using the formula of Byar [see Rothman and Boice (24)]. For duration of employment and latency analyses, significance factors (25) were used to assess the statistical significance of the SMR.

For SMR analyses by exposure frequency, we defined three groups: exposed daily (DE), exposed less than daily (LD), and nonexposed (NE). Person-years were assigned to the highest accrued frequency group. DE person-years include all person-years after first assignment into the DE group. LD person-years would include all person-years after an LD entry until a DE work history entry is encountered. NE person-years include only person-years until an LD or DE entry is encountered. For SMR analyses in the driver category, a slightly different strategy was used. All person-years and deaths were assigned to a driver from the date of accruing 1 year of marketing/distribution employment. Generally, there was very little movement in and out of the driver category, so the error introduced by this method of person-year assignment is likely to be minimal, although the direction of the error will result in underestimating the true SMR.

SMR analyses in occupational cohorts typically demonstrate the healthy worker effect, which results in a lower mortality than the general population. SMRs are not strictly comparable among different subcohorts of a population because the age standardization uses weights from the particular subcohort. If age distributions vary markedly, or overlap little, SMRs are truly noncomparable. To guard against these two weaknesses, we also used Poisson regression techniques to examine the effect of exposure.

In the Poisson regression analysis, the follow-up period was stratified into four time periods each 5 years long: a) 1 January 1964 to 31 December 1968; b) 1 January 1969 to 31 December 1973; c) 1 January 1974 to 31 December 1978; and d) 1 January 1979 to 31 December 1983. Within each stratum, a cohort member was classified by each of six demographic (independent) variables shown in the appendix. Total person-years in the stratum was recorded for each member. If a member changed classification within a 5-year period, he or she was recorded in each classification with the appropriate person-years.

The three exposure frequency ratings (NE, LD, DE) were used as exposure variables. The data were analyzed using Poisson regression (26). The large number of combinations of the independent variables result in relatively few mortality incidents within a study stratum, and the Poisson regression technique is suited to this type of data. Analyses were run for mortality caused by the *a priori* causes (LH and kidney cancer), as well as other diseases that showed suggestive findings in SMR analyses. The analyses were conducted by fitting the Poisson model with exposure frequency and age data, then adding gender as an independent variable, adding SES, then adding period of year of employment, and lastly adding a variable indicating if the stratum was before or after 1974. In those cases when adding one or more of the potentially confounding variables resulted in large variances for the estimates of the coefficient, the variable was not entered in the equation.

Results

Overall Cohort

The cohort consists of 6672 employees who contributed 99,184 person-years of observation over the 20-year study period, for an average of 14.8 years of follow-up for each employee. Table 2 displays several characteristics of the cohort. The birth year for the cohort ranged from 1873 to 1964, with the median birth year being 1931. Slightly more than half of the cohort achieved the 1-year worked criteria in marketing/distribution during the 1960s and 1970s, but nearly one-third started marketing/distribution work in the 1940s and 1950s as well. Twenty-seven percent of the cohort was active at the end of follow-up; 55% had terminated employment. Sixty percent of the terminated employees did so between 1965 and 1974. At the end of the follow-up period, 1154 men (17%) had died; thus this is a relatively young cohort. The length of employment distribution showed that one fifth of the employees worked less than 5 years, and 58% worked for 15 years or more. The median length of employment was 18 years. The average age of entry into follow-up was 38, and the average year of entry was 1967, with over half entering in 1964, the year follow-up commenced.

Table 3 shows mortality results for the overall cohort. Over the 20-year period, 1154 deaths were observed, with 1301 expected (E), yielding an all-cause SMR of 0.88. The 95% CI was 0.84, 0.94, indicating a significantly low mortality rate. The SMR for all cancer was 0.90 (95% CI =

Table 2. Characteristics of the overall cohort.

Characteristic	Number	Percent
Year of birth		
<1900	522	8
1900-09	548	8
1910-19	748	11
1920-29	1265	19
1930-39	1490	22
1940-49	1471	22
1950 +	628	9
Total	6672	100
Year of achieving 1 year employment in distribution		
1900-19	150	2
1920-29	437	7
1930-39	449	7
1940-49	940	14
1950-59	1196	18
1960-69	1897	28
1970 +	1603	24
Total	6672	100
Status on 31 Dec., 1983		
Active	1825	27
Dead	1154	17
Terminated	3693	55
Total	6672	100
Length of employment		
1-4	1341	20
5-14	1473	22
15-24	1282	19
25-34	1674	25
35 +	902	14
Total	6672	100

0.79, 1.02), based on 254 deaths. Only one cause of death was significantly elevated – aortic aneurysms ($O = 25$, $SMR = 1.79$, 95% $CI = 1.15, 2.64$). Two other causes had higher SMRs, but because fewer deaths were involved, neither cause was statistically significant. These were malignant melanoma ($O = 6$, $SMR = 2.63$, 95% $CI = 0.96, 5.73$), and multiple myeloma ($O = 7$, $SMR = 1.83$, 95% $CI = 0.73, 3.77$).

Two causes of *a priori* interest, leukemia and kidney cancer, showed identical SMRs of 1.35. There were 9 kidney cancer deaths (95% $CI = 0.62, 2.57$), and 14 leukemia deaths (95% $CI = 0.74, 2.26$). The only other cancer subsites with SMRs greater than 1.0 are esophageal cancer ($O = 9$, $SMR = 1.40$, 95% $CI = 0.63, 2.65$), cancer of the large intestine ($O = 31$, $SMR = 1.22$, 95% $CI = 0.83, 1.73$), prostate cancer ($O = 28$, $SMR = 1.08$, 95% $CI = 0.72, 1.56$), and brain cancer ($O = 7$, $SMR = 1.01$).

Hydrocarbon Exposure

Of the 6672 employees who worked in downstream for at least 1 year, 4889 employees (73%) were ever exposed to hydrocarbons. Table 4 shows mortality results for employees with HC exposure in the marketing/distribution segment. For the most part, mortality patterns closely parallel those of the total cohort. The person-year distribution by age of both cohorts is nearly identical; thus, the slight difference in weights used in the SMR calculation have a negligible effect on the SMR contrasts between these two populations. Mortality for all causes, total cancer, and circulatory disease is similar in the exposed group.

Table 3. Standardized mortality ratios (SMRs) for all marketing distribution workers.^a

Causes of death	Observed	Expected	SMR	95% C.I.
All causes of death	1154	1301.4	0.88	0.84, 0.94
All malignant neoplasms	254	282.8	0.90	0.79, 1.02
Esophageal cancer	9	6.5	1.40	0.63, 2.65
Stomach cancer	18	23.9	0.76	0.45, 1.19
Large intestinal cancer	31	25.5	1.22	0.83, 1.73
Rectal cancer	6	11.7	0.51	0.19, 1.11
Pancreatic cancer	15	16.2	0.93	0.52, 1.53
Lung/bronchus cancer	64	82.0	0.78	0.60, 1.00
Malignant melanoma	6	2.3	2.63	0.96, 5.73
Prostatic cancer	28	25.9	1.08	0.72, 1.56
Bladder cancer	5	9.6	0.52	0.17, 1.22
Kidney cancer	9	6.6	1.35	0.62, 2.57
Brain cancer	7	6.9	1.01	0.41, 2.08
Non-Hodgkin's lymphoma	7	7.6	0.92	0.37, 1.90
Reticulum cell sarcoma	1	1.7	0.58	—
Lymphosarcoma	2	2.4	0.83	—
Multiple myeloma	7	3.8	1.83	0.73, 3.77
All leukemias	14	10.4	1.35	0.74, 2.26
Myeloid/lymphatic leukemia	7	7.2	0.98	0.39, 2.02
Benign neoplasms	1	1.1	0.95	—
Circulatory diseases	650	664.3	0.98	0.90, 1.06
Myocardial infarction	229	235.2	0.97	0.85, 1.11
Aortic aneurysm	25	14.0	1.79	1.15, 2.64
Respiratory diseases	66	93.2	0.71	0.55, 0.90
Digestive diseases	35	54.0	0.65	0.45, 0.90
Kidney diseases	14	13.2	0.68	0.31, 1.29
External causes	72	113.8	0.63	0.49, 0.80

^aTotal person-years: 99,185.

Table 4. Standardized mortality ratios (SMRs) for marketing distribution workers exposed to hydrocarbons.^a

Causes of death	Observed	Expected	SMR	95% C.I.
All causes of death	767	854.6	0.90	0.83, 0.96
All malignant neoplasms	176	186.4	0.94	0.81, 1.09
Esophageal cancer	6	4.3	1.41	0.51, 3.07
Stomach cancer	12	15.5	0.77	0.40, 1.35
Large intestinal cancer	25	16.7	1.50	0.97, 2.21
Rectal cancer	5	7.7	0.65	0.21, 1.52
Pancreatic cancer	12	10.7	1.13	0.58, 1.97
Lung/bronchus cancer	43	54.6	0.79	0.57, 1.06
Malignant melanoma	4	1.6	2.49	0.67, 6.36
Prostatic cancer	19	16.3	1.17	0.70, 1.82
Bladder cancer	3	6.1	0.49	0.09, 1.43
Kidney cancer	7	4.4	1.58	0.63, 3.25
Brain cancer	4	4.8	0.83	—
Non-Hodgkin's lymphoma	4	5.1	0.78	0.21, 2.00
Reticulum cell sarcoma	0	1.2	0	—
Lymphosarcoma	2	1.6	1.25	—
Multiple myeloma	5	2.5	1.99	0.64, 4.63
All leukemias	7	6.9	1.01	0.40, 2.08
Myeloid/lymphatic leukemia	4	4.8	0.84	—
Benign neoplasms	1	0.7	1.41	—
Circulatory diseases	411	430.2	0.96	0.86, 1.05
Myocardial infarction	155	155.8	1.00	0.84, 1.16
Aortic aneurysm	11	9.0	1.22	0.61, 2.19
Respiratory diseases	41	59.5	0.69	0.49, 0.94
Digestive diseases	28	36.4	0.76	0.51, 1.11
Kidney diseases	7	8.5	0.82	0.33, 1.69
External causes	56	81.0	0.69	0.52, 0.90

^aTotal person-years: 71,776.

For the *a priori* causes there were slight differences in mortality between the total group and those exposed to hydrocarbons. For kidney cancer, the SMR showed a slight increase in the exposed workers ($O = 7$, $SMR = 1.58$, $95\% \text{ CI} = 0.63, 3.25$) relative to all workers ($O = 9$, $SMR = 1.35$). For leukemia, the SMR dropped from 1.35 in all workers to 1.01 in the exposed workers. For multiple myeloma, similar mortality was evident in exposed workers ($O = 5$, $SMR = 1.99$) versus all workers ($O = 7$, $SMR = 1.83$). The CI for the multiple myeloma SMR in exposed workers shows a slight loss of precision ($95\% \text{ CI} = 0.64, 4.63$) and includes the null value of 1.0.

Most other cancer causes of death showed similar results for the exposed workers compared to the total cohort. The SMR for malignant melanoma was similar in exposed workers 2.49 ($O = 4$) compared to all workers 2.63 ($O = 6$). The only cancer SMR that showed a moderate increase in the exposed population based on a reasonable number of deaths was that for cancer of the large intestine, which increased from 1.22 to 1.50 ($95\% \text{ CI} = 0.97, 2.21$) in exposed workers.

The aortic aneurysm SMR was not significant in HC-exposed workers as it was in the total workforce. This cause of death showed an SMR of 1.22 in exposed workers based on only 11 deaths. Thus, the aortic aneurysm excess is more evident in employees not exposed to HC. Only 44% of the aortic aneurysm decedents were defined as ever exposed, compared to 73% of all workers.

Exposure Frequency

Next we examined results by exposure frequency group. In these analyses, employees were classified according to their highest attained exposure frequency group ($DE > LD > NE$). Table 5 shows SMRs by exposure frequency. For most of the broader cause-of-death categories, (i.e., all causes, all cancer, myocardial infarction, respiratory disease, and external causes), a characteristic pattern of SMRs is apparent. The LD group shows the lowest SMRs, followed by the NE group, while the DE group shows the highest SMRs. However, the confidence intervals around the SMRs usually overlap, and the magnitude of the SMR differences is usually not large. Some exceptions are noted below.

For the leukemias, the highest mortality ($SMR = 2.00$) is in the unexposed group. The SMRs for the LD and DE groups are very imprecise, but there appears to be no pattern in risk in relation to the frequency of hydrocarbon exposure. For kidney cancer, imprecise SMRs near 1.0 are present in the NE and LD groups, whereas the daily exposed SMR is 2.08 ($95\% \text{ CI} = 0.67, 4.85$) based on five deaths. Again, the numbers of deaths are extremely small, limiting a precise interpretation of this pattern.

None of the other LH cancers seems to be strongly related to exposure frequency. There are no deaths due to non-Hodgkin's lymphoma in the DE group. Multiple myeloma SMRs are not strongly related to exposure fre-

Table 5. Standardized mortality ratios (SMRs) by exposure frequency.^a

Causes of death	Exposure frequency								
	Nonexposed			Less than daily			Daily		
	O/E	SMR	95% C.I.	O/E	SMR	95% C.I.	O/E	SMR	95% C.I.
All causes	387/446.8	0.87	0.78, 0.96	363/436.3	0.83	0.75, 0.92	404/418.8	0.97	0.87, 1.06
All cancers	78/96.4	0.81	0.64, 1.01	69/89.9	0.77	0.60, 0.97	107/96.5	1.11	0.91, 1.34
Esophagus cancer	3/2.2	1.36	—	5/2.0	2.47	0.80, 5.77	1/2.2	0.45	—
Stomach cancer	6/8.4	0.71	0.26, 1.55	4/7.9	0.51	0.14, 1.30	8/7.6	1.05	0.45, 2.07
Large intestine cancer	6/8.8	0.68	0.25, 1.48	13/8.4	1.55	0.83, 2.66	12/8.3	1.45	0.75, 2.53
Rectum cancer	1/4.0	0.25	—	1/3.9	0.26	—	3/3.8	0.79	—
Pancreas cancer	3/5.5	0.55	0.11, 1.59	5/5.1	0.98	0.32, 2.29	7/5.6	1.26	0.50, 2.59
Lung cancer	21/27.4	0.77	0.47, 1.17	12/24.3	0.49	0.26, 0.86	31/30.3	1.02	0.70, 1.45
Melanoma cancer	2/0.7	2.86	—	2/0.7	2.86	—	2/0.9	2.20	—
Prostate cancer	9/9.6	0.94	0.43, 1.78	7/9.5	0.74	0.30, 1.52	12/6.8	1.77	0.92, 3.09
Bladder cancer	2/3.5	0.57	—	0/3.3	0	—	3/2.8	1.07	—
Kidney cancer	2/2.2	0.91	—	2/2.0	0.99	—	5/2.4	2.08	0.67, 4.85
Brain cancer	3/2.1	1.43	—	1/2.0	0.50	—	3/2.9	1.05	—
Non-Hodgkin's lymphoma	3/2.5	1.20	—	4/2.4	1.70	—	0/2.8	0	—
Reticulosarcoma	1/0.5	2.00	—	0/0.5	0	—	0/0.6	0	—
Lymphosarcoma	0/0.8	0	—	2/0.8	2.64	—	0/0.8	0	—
Multiple myeloma	2/1.3	1.54	—	2/1.2	1.67	—	3/1.3	2.28	—
Leukemias	7/3.5	2.00	0.80, 4.12	2/3.4	0.59	—	5/3.5	1.42	0.46, 3.32
Myeloid/lymphoid leukemia	3/2.4	1.25	—	2/2.3	0.85	—	2/2.4	0.83	—
Benign neoplasm	0/0.4	0	—	0/0.3	0	—	1/0.4	2.64	—
Circulatory disease	239/234.1	1.02	0.90, 1.16	220/228.2	0.96	0.84, 1.10	191/202.1	0.95	0.82, 1.09
Myocardial infarction	74/79.4	0.93	0.73, 1.17	64/73.1	0.88	0.68, 1.12	91/82.7	1.10	0.89, 1.35
Aortic aneurysm	14/5.0	2.80	1.53, 4.70	7/4.6	1.52	0.61, 3.13	4/4.4	0.91	—
Respiratory diseases	25/33.7	0.74	0.48, 1.10	16/33.1	0.48	0.28, 0.79	25/26.4	0.95	0.61, 1.40
Digestive diseases	7/17.6	0.40	0.40, 0.82	16/17.1	0.94	0.54, 1.52	12/19.3	0.62	0.32, 1.08
Kidney diseases	7/4.7	1.49	0.60, 3.07	6/4.8	1.26	0.46, 2.75	1/3.8	0.27	—
External causes	16/32.8	0.49	0.23, 0.79	13/36.4	0.36	0.19, 0.61	43/44.7	0.96	0.70, 1.30

^aPerson-years at risk: nonexposed, 27,409; less than daily, 31,159; daily, 40,708.

quency, although the DE SMR of 2.28 is slightly higher than those in the other two groups (1.54 for NE, 1.67 for LD). Again, the SMRs for the exposure frequency groups are unstable due to small numbers.

As previously noted, the SMR for cancer of the large intestine was higher in the exposed group. The exposure frequency analyses show that this is due to slightly raised mortality in both the LD (O = 13, SMR = 1.55) and DE (O = 12, SMR = 1.45) groups. Rectal cancer, however, shows a higher SMR in the DE group only, although all rectal cancer SMRs are below 1.0, and there are only five deaths. The only other cancer site that merits mention is prostate cancer, which shows a moderately raised SMR (1.77) based on 12 cases in the DE group only.

The exposure frequency analyses underscore the lack of an effect due to hydrocarbons on aortic aneurysm mortality. There is a significant excess of aortic aneurysms (O = 14, SMR = 2.80) in the nonexposed group. The SMRs drop markedly in the LD (O = 7, SMR = 1.52) and the DE (O = 4, SMR = 0.91) groups. Further investigation of the work histories of the 14 nonexposed deaths revealed no unusual clustering by job, location, or department. Jobs represented more than once included plant superintendent (4) and clerk (4). Several diverse locations were represented, with only London, Ontario, and Edmonton, Alberta, occurring twice.

Latency and Duration of Employment

Next we examined selected cancer causes by latency and duration of employment. Latency is measured from the

time of first exposure, and employment duration is measured from date first employed in marketing/distribution. Table 6 shows the results for duration of employment while imposing a 10-year latency criteria for cancer causes of interest.

For kidney cancer, there is a concentration of deaths in the 20–29 years worked category but not in the 30+ category. The small number of deaths precludes a definitive interpretation. For leukemia, no increasing trend in the SMR is evident for longer employment duration. The same is true for non-Hodgkin's lymphoma. Again, the small number of deaths in these analyses makes a clear interpretation impossible.

Multiple myeloma deaths do concentrate in longer-tenured employees. Both the 20–29 and 30+ years employed groups show over a 2-fold risk as measured by the SMR. However, these measures are based on few deaths, and neither is statistically significant.

Only two melanoma deaths survived a 10-year latent period; thus, no trend with employment duration can be evaluated. For other cancers, only two show suggestive relationships with tenure. The first is esophageal cancer, in which a nearly 3-fold risk is evident for the 30+ year group based on four cases. The other is cancer of the large intestine. The 30+ year group showed a statistically significant SMR of 2.33 based on 13 cases. The other three employment categories (<10, 10–19, 20–29) showed essentially equal SMRs slightly above 1.0.

Because rectal cancer and large intestine cancer share several risk factors and are often categorized together for etiologic studies, it is interesting to note the rectal cancer

Table 6. Cancer standardized mortality ratios (SMRs) by length of employment for latency 10 years after first exposure.

Causes of death	Years employed							
	<10		10-19		20-29		30 +	
	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR
Esophageal cancer	0	0	1	1.14	1	0.63	4	2.95
Stomach cancer	1	1.69	2	0.67	4	0.69	5	0.96
Large intestine cancer	1	1.40	4	1.26	7	1.13	13	2.33*
Rectal cancer	0	0	2	1.34	2	0.70	0	0
Pancreatic cancer	0	0	4	1.87	5	1.30	1	0.29
Lung/bronchus cancer	3	1.01	7	0.62	16	0.83	16	0.91
Melanoma	0	0	1	2.37	1	2.42	0	0
Prostatic cancer	1	3.15	4	1.78	5	0.73	8	1.22
Bladder cancer	0	0	1	1.00	0	0	2	0.86
Kidney cancer	0	0	1	1.02	4	2.60	1	0.75
Brain cancer	0	0	1	0.77	1	0.74	2	2.14
Non-Hodgkin's lymphoma	0	0	1	2.23	1	0.61	0	0
Multiple myeloma	0	0	0	0	2	2.21	2	2.31
All leukemias	0	0	2	1.44	3	1.32	1	0.50
Myeloid/lymphoid leukemia	0	0	1	0.97	2	1.56	0	0

* $p < 0.05$.

results. SMRs for rectal cancer show no (or possibly an inverse) trend with years employed. The combined category of colorectal cancer shows an SMR of 1.60 based on 13 cases for the 30 + year grouping, which is not statistically significant.

In another analysis, we also imposed a 20-year latency period while calculating SMRs for the same employment duration groups. For the most part, the employment duration results were unchanged for the 20-year latency restriction. The only material difference was that the bronchus/lung cancer SMRs were directly related to employment duration, but all SMRs indicated mortality rates below the referent population. The bronchus/lung cancer SMRs for the four duration of employment groups were 0, 0.56, 0.83, and 0.91.

When we examined results by a 10- and 20-year latent period (as defined from first exposure in marketing/distribution), only cancer of the large intestine showed a statistically significant risk for a latent period of 10 years ($O = 25$, $SMR = 1.60$) (Table 7). A 20-year latency period

produced a similar risk of borderline statistical significance. Other moderately raised risks were seen for a latent period of 10 years, including esophageal cancer ($O = 6$, $SMR = 1.49$), malignant melanoma ($O = 2$, $SMR = 1.55$), kidney cancer ($O = 6$, $SMR = 1.46$), and multiple myeloma ($O = 4$, $SMR = 1.69$). For these diseases, a latent period of 20 years produced a similar risk for esophageal cancer and a lower risk for malignant melanoma, the latter based on only one case. SMRs for kidney cancer and multiple myeloma were higher when imposing a 20-year latent period ($O = 6$, $SMR = 1.81$; $O = 4$, $SMR = 1.97$, respectively).

Tank Truck Drivers

Because tank truck drivers have a well-described pattern of hydrocarbon exposure and other studies have examined this group of workers, we defined a category of "ever drivers" to examine mortality patterns. Table 8 shows the mortality experience of drivers. Overall mor-

Table 7. Cancer standardized mortality ratios (SMRs) for latent periods 10 and 20 years after first exposure.^a

Cancer type	Latency > 10 years			Latency > 20 years		
	Observed	Expected	SMR	Observed	Expected	SMR
Esophageal	6	4.0	1.49	5	3.4	1.47
Stomach	12	14.6	0.82	10	12.6	0.79
Large intestinal	25	15.7	1.60*	21	13.5	1.55
Rectal	4	7.2	0.55	4	6.2	0.65
Pancreatic	10	10.0	1.00	8	8.5	0.95
Lung/bronchus	42	51.2	0.82	35	42.6	0.82
Malignant melanoma	2	1.3	1.55	1	0.8	1.22
Prostatic	18	14.4	1.25	18	13.7	1.31
Bladder	3	5.9	0.51	3	5.4	0.55
Kidney	6	4.1	1.46	6	3.3	1.81
Brain	4	4.0	0.99	3	2.7	1.11
Non-Hodgkin's lymphoma	4	4.5	0.88	2	3.5	0.57
Multiple myeloma	4	2.4	1.69	4	2.0	1.97
All leukemias	6	6.1	0.99	6	4.9	1.22
Myeloid/lymphoid leukemia	3	4.2	0.72	3	3.3	0.90

^aPerson-years at risk: 45,629 for > 10 years latency; 23,804 for > 20 years latency.* $p < 0.05$.

Table 8. Standardized mortality ratios (SMRs) for tank truck drivers employed more than 1 year.^a

Cause of death	Observed	Expected	SMR	95% C.I.
All causes of death	157	174.5	0.90	0.76, 1.05
All malignant neoplasms	32	37.7	0.85	0.58, 1.20
Esophageal cancer	2	0.9	2.31	—
Stomach cancer	3	3.0	1.03	—
Large intestinal cancer	2	3.2	0.62	—
Rectal cancer	0	1.5	0	—
Pancreatic cancer	3	2.1	1.41	—
Lung/bronchus cancer	9	11.4	0.79	0.36, 1.50
Malignant melanoma	0	0.5	0	—
Prostatic cancer	2	2.5	0.80	—
Bladder cancer	2	1.0	1.92	—
Kidney cancer	2	1.0	2.10	—
Brain cancer	0	1.3	0	—
Non-Hodgkin's lymphoma	0	1.2	0	—
Reticulum cell sarcoma	0	0.3	0	—
Lymphosarcoma	0	0.3	0	—
Multiple myeloma	1	0.5	2.01	—
All leukemias	5	1.5	3.35	1.08, 7.81
Myeloid/lymphoid leukemia	4	1.0	3.87	1.06, 9.92 ^b
Benign neoplasms	1	0.2	6.19	—
Circulatory diseases	71	81.3	0.87	0.68, 1.10
Myocardial infarction	41	32.4	1.27	0.91, 1.72
Aortic aneurysm	1	1.5	0.65	—
Respiratory diseases	8	10.5	0.77	0.33, 1.51
Digestive diseases	8	8.6	0.93	0.40, 1.84
Kidney diseases	2	1.6	1.24	—
External causes	28	23.5	1.19	0.79, 1.72
Motor vehicle accidents	12	7.0	1.73	0.89, 3.01

^aTotal person-years: 21,942.^bFisher's exact formula used.

tality is nearly identical to the whole cohort of marketing/distribution workers. Circulatory disease mortality is slightly lower in drivers (SMR = 0.87); however, mortality from acute myocardial infarction shows an elevation ($O = 41$, SMR = 1.27) but is not quite statistically significant (95% CI = 0.91, 1.72). The excess of aortic aneurysm in the total cohort is not evident in drivers. As expected, the SMR for motor vehicle traffic accidents is somewhat elevated in these drivers ($O = 12$, SMR = 1.73, 95% CI = 0.89, 3.01).

Both kidney cancer and leukemia showed increased mortality in drivers. The kidney cancer SMR of 2.10 is quite imprecise (Fisher's exact 95% CI = 0.24, 7.57) and far from statistically significant. Five total leukemias among drivers resulted in an SMR of 3.35, which is statistically significant according to the 95% CI of 1.08, 7.81. The lymphatic and myeloid combined category is also significant (SMR = 3.87) based on four cases and a 95% CI (Fisher's exact) of 1.06, 9.92. Of these deaths, three were due to myelocytic leukemia (one acute, one chronic, and one unspecified as to acute or chronic). The other death was simply classified as acute leukemia (code 204.3 in the 7th revision of the ICD) and was unspecified as to whether the cell type was of lymphocyte, myelocyte, or mixed origin.

We examined leukemia SMRs in truck drivers by length of employment for workers who satisfied a 10-year latency criteria. Four of the five observed deaths and 1.2 of the 1.5 expected deaths satisfied the 10-year latency criteria for an SMR of 3.23 and a 95% (exact) CI of 0.88, 8.27. For <10, 10–19, 20–29, and 30+ employment groups, the SMRs are 0, 4.85, 3.92, and 0. Thus, a strong trend of increasing risk

with tenure is not apparent in tank truck drivers, although small numbers limit the detection of such trends.

Most other SMRs are imprecise due to the relatively small number of drivers in this study. One multiple myeloma and two esophageal cancers were observed, and although the SMR's are above 2.0 for these causes, they are extremely imprecise due to the small number of expected deaths.

Modeling

To further investigate possible effects of hydrocarbon exposure while controlling for other variables of interest, we used Poisson regression to model the death rate due to specific causes on different explanatory variables. The advantage of this technique includes the fact that variables not controlled for in the national rates can be used, and the healthy worker effect should be eliminated by using the nonexposed group as the referent population. In addition to age and time, which were controlled in the SMR and Poisson regression analyses, we used two other variables: socioeconomic status (SES), which was based on job classification, and period of hire.

Generally, the modeling techniques confirmed the analyses by exposure frequency presented in Table 5. For leukemia and total LH cancers, relative risks for the LD and DE exposure frequency groups were lower than 1.0 (Table 9). Various combinations of explanatory variables (i.e., controlling for age; age and SES; age, SES, and year hired; or age, SES, year hired, and time) did not markedly alter these results. Modeling results for exposure fre-

Table 9. Relative risks by exposure frequency based on Poisson regression model and 95% confidence intervals.

Cause of death	Exposure frequency	Relative risk (C.I.)			
		Age	Age + SES	Age + SES + year hired	Age + SES + year hired + pre/ post 1974
All lymphohematopoietic cancer	Less than daily	0.70 (0.28, 1.78)	0.80 (0.28, 2.29)	0.82 (0.29, 2.34)	0.84 (0.29, 2.43)
	Daily	0.76 (0.31, 1.88)	0.68 (0.23, 1.94)	0.82 (0.28, 2.37)	0.81 (0.28, 2.36)
Leukemia	Less than daily	0.33 (0.07, 1.59)	0.54 (0.10, 2.96)	0.58 (0.10, 3.17)	0.65 (0.12, 3.59)
	Daily	0.91 (0.29, 2.88)	0.61 (0.16, 2.38)	0.92 (0.22, 3.73)	0.90 (0.22, 3.64)
Multiple myeloma	Less than daily	a	0.65 (0.09, 4.81)	0.67 (0.09, 5.02)	a
	Daily	a	0.96 (0.15, 6.24)	1.23 (0.18, 8.56)	a
Kidney cancer	Less than daily	1.19 (0.17, 8.50)	0.75 (0.06, 10.15)	0.85 (0.06, 12.41)	0.84 (0.06, 12.17)
	Daily	2.84 (0.55, 14.72)	4.06 (0.58, 28.21)	3.86 (0.44, 33.67)	3.80 (0.45, 32.29)
Esophageal cancer	Less than daily	1.96 (0.47, 8.20)	2.44 (0.52, 11.59)	2.45 (0.52, 11.58)	a
	Daily	0.40 (0.04, 3.88)	0.32 (0.03, 3.50)	0.33 (0.03, 3.70)	a
Colorectal cancer	Less than daily	1.63 (0.72, 3.67)	1.66 (0.65, 4.22)	1.66 (0.66, 4.24)	1.69 (0.66, 4.34)
	Daily	1.24 (0.51, 2.98)	1.48 (0.54, 4.04)	1.51 (0.55, 4.16)	1.49 (0.54, 4.16)
Malignant melanoma	Less than daily	1.96 (0.33, 11.73)	1.57 (0.21, 11.60)	1.74 (0.24, 12.67)	1.74 (0.24, 12.73)
	Daily	0.49 (0.04, 5.44)	0.48 (0.03, 7.82)	0.53 (0.03, 8.60)	0.54 (0.03, 8.66)
Aortic aneurysm	Less than daily	0.70 (0.29, 1.69)	0.52 (0.20, 1.35)	0.52 (0.20, 1.37)	0.52 (0.20, 1.37)
	Daily	0.30 (0.08, 1.06)	0.21 (0.06, 0.76)	0.23 (0.06, 0.85)	0.23 (0.06, 0.86)

SES, socioeconomic status.

^aStandard error of estimated coefficient >10¹².

quency and multiple myeloma were generally unremarkable. Only when age, SES, and year hired were controlled did daily exposure to HCs increase the risk of multiple myeloma, but the magnitude of the relative risk (1.23) is low, and the confidence interval (0.18–8.56) is wide.

For all combinations of explanatory variables, the kidney cancer relative risks were moderately high for the daily exposed group. Although the SMR was 2.08, the relative risks are in the range of 3–4. However, the confidence intervals are extremely wide, indicating a very imprecise result.

Relative risks for colorectal cancer again show a moderate risk in the 1.2–1.7 range for both exposure frequency groups (less than daily and daily exposure) and various combinations of explanatory variables. Again, the value of 1.0 falls well within the range of the confidence intervals.

The aortic aneurysm relative risks show a significant reduction in risk for higher exposure frequency, a pattern also observed in the SMR analyses. Various combinations of explanatory variables do not alter this result.

Discussion

Strengths and Limitations

This study was undertaken to investigate the mortality patterns of a group of workers with exposure to various petroleum fuels. The advantages and disadvantages of the retrospective cohort mortality design are well known. Advantages include use of the modified life table method to calculate rates of disease with person-time denominators, which is superior to proportional mortality or cross-sectional designs. Mortality data are relatively easy to classify based on standard coding schemes.

The study also used extensive industrial hygiene expertise to classify the frequency of hydrocarbon exposure for various work history combinations of job, department, and location. These individuals were intimately familiar with the marketing/distribution environment, and we believe the exposure assignment task, though relying on industrial hygiene judgment, was accomplished with a high degree of validity for the criteria chosen.

While not formally tested, we believe that the inherent degree of accuracy necessary in payroll and benefits functions renders a high probability that the cohort is nearly complete. Death tracing is also reasonably complete and the fact that SC ICD codes were used for both this study population and the national statistics limits the possibility of inaccuracies due to nosologist coding preferences.

The weaknesses of this study include the reliance on mortality only (and not disease incidence) as the outcome, and the relatively small numbers of deaths in the study. The follow-up period is relatively short, and the cohort is relatively young, which translates into smaller numbers of expected deaths given the number of persons included in the study. Further follow-up of the cohort, which naturally will have aged, would be a useful adjunct to this study.

Counterbalancing the validity of the exposure assignment process is the lack of complete work histories for 50% of the cohort. In conducting a case-control study in the same group of workers, we were able to compare about 10 of the more complete manual work history records to the computerized record used in this study. The comparison indicated that the number of job changes was reduced by about 50% in the computerized history, although it was not possible to exactly determine a specific pattern of work history lines that were or were not included in the computerized record. We did not find any records that would indicate a change in exposure (from nonexposed to exposed), although these probably exist. We did find instances where the first exposure date was different on the two records. Thus, analyses by length of time from first exposure are characterized by some degree of misclassification.

For some employees, only the last job classification was available, and this represented the entire work history. We attempted to estimate the probable magnitude of this assumption by examining the employees with complete work histories. These are largely employees who started after 1964. For 930 employees with complete work histories whose last job was categorized as DE, 625 (67%) were always daily exposed, and 86% were daily exposed more than half the time. Similarly, for those exposed as LD, 50% were always exposed as LD, and 74% were exposed more than half the time as LD. Using a more detailed analysis, we estimate that 15% of DE time and 20% of LD time was misclassified. Of course, if this misclassification were non-differential (say for kidney cancer deaths versus all other employees), a dampening of a dose response would occur in this study, which would produce conservative estimates.

It was beyond the scope of this study to examine job titles, although this method can be very illuminating. The hundreds of unique job titles was somewhat surprising and indicates use of unique titles for different locations. We were able to examine drivers, who probably were among the more highly exposed individuals in the study due to the loading and unloading operations they frequently performed. This was possible because there were relatively few job titles that translated into the driver category. This analysis in effect offers an alternative means of evaluating HC exposures because the exposure frequency classification did not account for exposure intensity. Future analy-

ses would be strengthened by the examination of other job titles such as operators and mechanics.

Mortality for All Causes and Nonmalignant Causes of Death

Overall mortality in this cohort ($SMR = 0.88$) is significantly below the Canadian national mortality rate for a comparable population according to age, time period, and gender. For circulatory diseases, SMRs are 0.98 and 0.96 in all and HC-exposed workers, respectively. Myocardial infarction and aortic aneurysms also showed mortality higher than those normally seen in working populations. The major risk factors for heart disease include age, gender, cholesterol levels, smoking, and blood pressure. Other, less certain risk factors for cardiovascular disease include obesity and physical inactivity. Age and gender can of course be ruled out because they have been adjusted for in all analyses. One would expect to see high SMRs for lung cancer if this population smoked more than the general population, but these are not evident. In fact, due to the flammable fuels present in the work environment, smoking is restricted, which may result in less smoking than in the general population. We do not have data on cholesterol levels, blood pressure, or obesity in these workers relative to the general population. Physical inactivity may be higher for drivers, but they make up only 22% of this cohort.

One possible explanation for the slightly elevated circulatory disease SMRs is that approximately one-third of the population entered follow-up as annuitants; thus, the healthy worker effect may have dissipated. However, this explanation would require the diminishing impact of the healthy worker effect to apply to circulatory but not to respiratory or other nonmalignant diseases. Nevertheless, we examined both circulatory disease and myocardial infarction mortality in these older workers and found essentially identical SMRs to the whole cohort. In fact, the SMRs are higher for workers who entered follow-up after 1964 versus the whole cohort. For all circulatory disease, the after-1964 SMR is 1.30 ($O = 19$) versus 0.98 for all workers. For myocardial infarction, the after-1964 SMR is 1.35 ($O = 11$) versus 0.97 for all workers. Neither SMR is significant. These results are puzzling, and the study probably did not collect the relevant risk factor information to elucidate the patterns further. Thus, the reason underlying the slight elevation in circulatory disease and myocardial infarction remains unexplained.

Rushton and Alderson (3) reported remarkably similar results for ischemic heart disease (ICD codes = 410-414; $SMR = 0.99$) to our results for all circulatory disease (ICD codes 390-458) and myocardial infarction (ICD code 410). They investigated the pattern in several job classifications and did not come up with concise reasons for the lack of a healthy worker effect for this cause.

A Priori Causes

This study was conducted primarily to investigate the effect of two disease categories: the LH cancers, particu-

larly leukemia and multiple myeloma, and kidney cancer. For leukemia, the major finding was among truck drivers. This group showed a statistically significant SMR of 3.35. Nearly all other analyses suggested that the leukemia risk was not related to HC exposure. The SMR was higher for the nonexposed group, and the internal analyses showed risk ratios below 1.0 for both measures of exposure frequency. No trends were evident by latency and length of employment, although five of seven of the exposed workers in the duration of employment analysis were employed between 10 and 29 years.

There are a few explanations for this apparently conflicting result. First, the job categorization could offer a more precise measure of the underlying causal factor compared to the exposure frequency estimates. For example, the driver job may be a relatively accurate surrogate for peak-type exposure patterns. For this study, the truck drivers were mostly assigned to the DE exposure category, but a few were assigned to LD as well based on tasks performed. Second, there is always the possibility that uncontrolled confounding variables in these drivers are present. Other risk factors for leukemia include radiation, genetic predisposition, and possibly smoking. We did not collect information on these risk factors; thus, the possibility that they explain or are involved in the excess cannot be ruled out. Third, the finding could be the result of evaluating multiple disease outcomes in several ways; thus, multiple hypothesis testing cannot be entirely ruled out.

The biologic feasibility of this finding is enhanced by the relationship between leukemia (particularly AML) and exposure to high levels of benzene reported by previous studies (27). It is also known that benzene was usually present in gasoline (over the study time period) at relatively low levels. Because we do not have access to the death certificates, at this point we are only aware that there is one definite and three possible AMLs among the drivers. Much debate centers on the precise level of benzene that results in leukemia excesses (15). At this point, we have no knowledge concerning the actual levels of benzene experienced by these truck drivers. The five leukemia decedents were all employed as drivers in 1972 or before. Current improvements in loading/unloading technology may not have been in place for the majority of these drivers.

There are few other studies that have reported leukemia findings for persons exposed to finished petroleum products. The IARC working group (1) estimated an odds ratio of 5.1 (95% CI = 2.6, 9.8) for exposure to petroleum products in a hospital-based case-control study of non-lymphocytic leukemia (28). Exposure to petroleum products in the Brandt et al. (28) study derived from driver or service station attendant jobs. Schwartz (29) also reported a proportionate mortality ratio (PMR) of 3.28 ($p < 0.05$) for service station attendants. Rushton and Alderson (3) reported a leukemia SMR of only 1.04 in their study on distribution workers, although the analogous SMR for drivers only was not published. Updated findings due to be presented in the cohort (3) should further elucidate the risk for leukemia in these workers and possibly in drivers

as well. For now, there is little evidence either supporting or conflicting with this finding.

For other LH cancers, the non-Hodgkin's lymphomas generally show no relationship with HC exposure, tenure, or latency. Multiple myeloma showed patterns somewhat consistent with a workplace influence, though the small number of deaths limits precise interpretations. The SMRs are 1.54 and 1.67 for the NE and LD groups and show a moderate increase to 2.28 for those exposed to HC on a daily basis. The internal analyses, however, pointed to a somewhat diminished relative risk (RR = 1.23) controlling for age, SES, and year hired. The risk concentrated in employees with longer tenure and in those who started work before 1950 (not shown).

These data on multiple myeloma provide conflicting interpretations; some findings (*viz.*, the trend for tenure, the SMR for the DE group) suggest a possible workplace relationship, but the modeling results and the small numbers in general weaken the potential for a workplace result. There are few other results with which to compare this finding because multiple myeloma is usually reported under a fairly diverse group of other lymphatic cancers, including polycythemia vera, non-Hodgkin's lymphomas, and unspecified lymphomas. Some investigators (27,30) suggest a possible relationship to benzene exposure (particularly low exposures). Our data cannot rule out this possibility. Future studies should report this cancer separately from others in which it is commonly grouped to clarify its relationship to employment in general, particularly in petroleum-related work.

For kidney cancer, our results are largely equivocal with regard to a workplace effect on mortality from this disease. The overall result shows a slight elevation (SMR = 1.35), whereas the SMR for HC-exposed employees is moderately raised (SMR = 1.58). This is due to a 2-fold elevation in the SMR for daily-exposed workers. Poisson regression modeling results suggest a similar pattern, with a relative risk of 0.85 for less than daily exposure and 3.86 (95% CI = 0.44, 33.67) for daily exposure based on a model controlling for age, SES, and year hired. The risk also is moderately elevated for workers who survived either 10- or 20-year latent periods from first exposure and is concentrated (SMR = 2.60) in workers employed between 20 and 29 years. A 2-fold risk also was evident in truck drivers. However, all of the SMRs mentioned above are imprecise, and the null value of 1.0 falls well within the range of all of the confidence limits. Thus, though the patterns of risk are consistent with a possible risk due to HC exposure, the limited number of observed and expected deaths are only suggestive and do not allow a concise interpretation.

Other relevant kidney cancer studies include a population-based case-control study among renal cell cancer cases (31), in which a slight trend of increasing odds ratios was found for gas station attendants. Domiano et al. (32), however, found an odds ratio of only 0.53 for persons exposed to gasoline in a population-based case-control study. Siemiatycki et al. (33) also found a significantly elevated risk for exposure to jet fuel and aviation gasoline, although the two findings were largely driven by the same

exposed cases. The risk for "substantial exposure" to aviation gasoline was 3.9 (90% CI = 1.7, 8.8). A slightly raised SMR of 1.21 was found in the only other previously published retrospective cohort study (3). This cohort study also separately reported a slightly higher SMR of 1.71 in drivers based on 12 cases (34). In petroleum refineries in which a broader spectrum of HC exposures are found, most studies do not show a risk (35), including a nested case-control study that used reasonable exposure estimating techniques for nonaromatic gasoline distillates (21). In summary, slight excesses of kidney cancer seem to be found more frequently in studies that could entail exposure to finished fuels rather than refining operations, although the evidence is still rather weak. Because the magnitude of the effects are relatively small, only prolonged follow-up of large cohorts or large population-based case-control studies among groups in which exposure to fuels is not rare will clarify the question.

Other Causes

We found six deaths and an SMR of 2.63 for malignant melanoma in this cohort. The SMR was essentially unchanged in the exposed cohort and did not show trends with employment duration and latency. There were no melanomas in the tank truck drivers. The parent cohort, which included refinery and upstream populations, showed a statistically significant SMR of 2.0 (95% CI = 1.12, 3.31), which concentrated in upstream workers (SMR = 6.00, 95% CI = 2.19, 13.06). In the upstream population, strong trends by latency and duration of employment were evident, which is not the case in the present study. In the upstream population, intermittent sunlight exposure, and dermal hydrocarbon exposure were potential etiologic candidates.

These marketing and distribution workers have somewhat less of a potential for dermal exposure relative to employees of the upstream segment. Crude oil and natural gas would not be encountered in the marketing/distribution segment, thus the upstream findings may not be relevant to these workers. The lack of a strong pattern of risk according to exposure, employment, and latency, the lack of findings in other populations exposed to petroleum fuels (3), and the small numbers of observed and expected deaths leads one to argue against a causal interpretation.

For colon cancer, an interesting pattern of mortality emerges from this study. The SMR in those exposed to hydrocarbons is 1.50, with a fairly narrow 95% CI of 0.97, 2.21. SMR analyses by exposure frequency show essentially the same risk for those exposed on a less than daily basis (1.56) versus a daily (1.45) basis with somewhat less precise confidence intervals (approximately 0.8, 2.5). In addition, an elevated SMR for workers with 30+ years of employment was observed (SMR = 2.33, $p < 0.05$), and more moderate SMRs (1.55, 1.60) for persons who satisfied a 10- or 20-year latency criteria (from first exposure) were found. Taken at face value, these patterns may suggest a possible occupational influence (i.e., there is within-study consistency). However, the magnitude of the risks are

generally small to moderate. Thus, other potential risk factors (e.g., dietary factors) not controlled in these analyses may have an impact on the risk estimates. To estimate a possible geographic influence, we have used both Ontario and Quebec rates in lieu of Canada rates, and the overall colon cancer SMR drops from 1.22 (Canadian rates) to 1.16 (Ontario rates) to 1.07 (Quebec rates). Thus, rates of colon cancer relevant to this cohort appear to be higher in Quebec and Ontario, which contain about half of the locations in this study.

Findings of elevated SMRs for cancer of the large intestine in the exposed and 30+ tenure groups are generally inconsistent with the other large scale published study (3) on marketing/distribution workers, which reported a significantly low SMR of 0.79 for this cause. In addition, most refinery worker studies report SMRs below 1.0 for this cause of death (8-13,36). Only Hanis et al. (36) reported a significant risk (standardized risk ratio = 1.97) in refinery workers (some of whom were among the parent cohort to this study). A chronic bioassay on unleaded gasoline with a 2% benzene content (17) did not report any histopathology effects or necropsy findings relevant to the large bowel in Fischer 344 rats or B₆C₃F₁ mice. Also, it is difficult to envision the biologic relevancy of inhalation exposure to hydrocarbon vapors having a unique effect on the colon. The lack of similar findings for rectal cancer in this study also argues against the biologic plausibility of the findings. However, the finding deserves increased scrutiny in future follow-up efforts in this cohort, as well as other cohorts with potential exposure to finished petroleum products.

The lack of a strong healthy worker effect in truck drivers in this study is somewhat perplexing. Company drivers undergo comprehensive physical exams to qualify as a driver, and additional examinations to qualify as a driver in this company. The provincial ministries of transportation guidelines require a comprehensive health examination, which must be taken to qualify for a Class A license and possible employment as a truck driver. In addition, the company requires a yearly examination of truck drivers and follows the Canadian Medical Association's Physician's Guide to Driver Examination (37), which specifies examination of each body system to measure possible impairment. Thus, procedures in place would seem to indicate an initial selection and ongoing maintenance of health that may exceed that for the general workforce. However, overall mortality is quite comparable to the balance of the cohort, although myocardial infarction mortality is higher than what is commonly seen in employed cohorts.

With a relatively sparse database among distribution workers, most of these results should be considered hypothesis generating and the impetus for future studies in these occupational groups. This population and others in the marketing/distribution segment are valuable for continuing the study of the health effects, or lack thereof, of fossil fuels and other petroleum products on health.

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Appendix

Demographic classification variables for modeling

Characteristic	Values	Model variable ^a
Gender	Male Female	Baseline SEXF = 1
Socioeconomic status	Employment classification < 21 Employment classification ≥ 21 and ≤ 23 Employment classification > 23	Baseline SES2 = 1 SES3 = 1
Hire year	Hired pre-1934 Hired between 1935 and 1963 inclusive Hired post-1964	Baseline HIRE2 = 1 HIRE3 = 1
Age, years ^b	Age < 45 Age 45–54 Age 55–64 Age > 64	Baseline AGE2 = 1 AGE3 = 1 AGE4 = 1
Exposure frequency	Not exposed in the stratum Exposed less than daily in the stratum Exposed daily in the stratum	Baseline EXPOSE2 = 1 EXPOSE3 = 1
Exposure class	Not exposed or less than daily for less than 5 years Exposed daily for 1–14 years, or exposed less than daily for 5 years or more Exposed daily for 15 years or more	Baseline DAILYLO = 1 DAILYHI = 1

^aOnly one flag can be used per classification.

^bAt start of stratum.